DEPARTMENT OF HEALTH & HUMAN SERVICES
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January 12, 2016

BIOPHOR DIAGNOSTICS, INC.
NATHANIEL BUTLIN, PH.D.
VICE PRESIDENT
1201 DOUGLAS AVE
REDWOOD CITY CA 94063

Re: K141748
Trade/Device Name: RapidFRET Oral Fluid Assay for Amphetamine,
RapidFRET Oral Fluid Amphetamine Calibrator Set,
RapidFRET Oral Fluid Amphetamine Control Set
Regulation Number: 21 CFR 862.3100
Regulation Name: Amphetamine test system
Regulatory Class: II
Product Code: DKZ, DLJ, LAS
Dated: April 27, 2015
Received: April 30, 2015

Dear Dr. Nathaniel Butlin:

This letter corrects our substantially equivalent letter of May 20, 2015.

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801).

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801) please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Courtney H. Lias -S

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k141748

Device Name
RapidFRET Oral Fluid Assay for Amphetamine
RapidFRET Oral Fluid Amphetamine Calibrator Set
RapidFRET Oral Fluid Amphetamine Control Set

Indications for Use *(Describe)*

The RapidFRET Oral Fluid Assay for Amphetamine is a homogeneous time-resolved fluorescence assay that is intended for prescription use in central laboratories only on the RapidFRET Integrated Workstation. The assay is used to perform a qualitative screen for amphetamine at 50 ng/mL in neat oral fluid samples collected with the RapidEASE Oral Fluid Collector. This assay provides only a preliminary result. To obtain a confirmed analytical result, a more specific alternate chemical method such as GC/MS or LC/MS/MS is required. Professional judgment should be applied to any drug test result, particularly when using preliminary positive results. For In Vitro Diagnostic Use Only.

The RapidFRET Oral Fluid Amphetamine Calibrator Set and RapidFRET Oral Fluid Amphetamine Control Set are intended for use only with the RapidFRET Oral Fluid Assay for Amphetamine and samples collected with the RapidEASE Oral Fluid Collector. The cutoff calibrator is used to determine the cutoff level and translate the assay measurement into a positive or negative result. The positive and negative controls are used to monitor laboratory systems, operators, precision, accuracy and assay conditions. For In Vitro Diagnostic Use Only.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary for the RapidFRET Oral Fluid Assay for Amphetamine

Preparation Date: May 13, 2014

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92

The assigned 510(k) number is: K141748

807.92(a)(1): Contact Information

Name: Biophor Diagnostics, Inc.
Address: 1201 Douglas Avenue
Redwood City, CA 94063

Contact: Nathaniel G. Butlin, Ph.D.
Phone: 650-367-4954
Fax: 650-364-4985

807.92(a)(2): Device Name, Common Name and Classification

RapidFRET Oral Fluid Assay for Amphetamine (Enzyme Immunoassay for Amphetamine)
RapidFRET Oral Fluid Amphetamine Calibrator Set (Clinical Toxicology Calibrator)
RapidFRET Oral Fluid Amphetamine Control Set (Drug Mixture Control Materials)

Product	Code	Class	Regulation Section	Panel
RapidFRET Oral Fluid Assay for Amphetamine	DKZ	II	862.3100	91 - Toxicology
RapidFRET Oral Fluid Amphetamine Calibrator Set	DLJ	II	862.3200	91 - Toxicology
RapidFRET Oral Fluid Amphetamine Control Set	LAS	I, Reserved	862.3280	91 - Toxicology

807.92(a)(3): Identification of Legally Marketed Predicate Devices

Roche Diagnostics DAT Oral Fluid Amphetamine (k110446).

807.92(a)(4): Device Description

The RapidFRET Oral Fluid Assay for Amphetamine is an In Vitro Diagnostic competitive immunoassay used to detect amphetamine in human oral fluid. This is a ready-to-use homogenous system that involves energy transfer between an acceptor fluorophore labeled to an antibody and a donor fluorophore labeled to drug. The assay is based on competition between drug in the sample and drug labeled with the donor fluorophore for a fixed number of binding sites on the antibody reagent. When acceptor and donor fluorophores

are brought into close proximity through a binding event, energy transfer occurs. The fluorescence resonance energy transfer (FRET) signal is measured at the wavelength of the acceptor fluorophore and is inversely proportional to the amount of drug in the sample. A Cutoff Calibrator is used to translate the sample measurement into a positive or negative result. Controls are used to establish and monitor precision and accuracy.

807.92(a)(5): Intended Use

The RapidFRET Oral Fluid Assay for Amphetamine is a homogeneous time-resolved fluorescence assay that is intended for prescription use in central laboratories only on the RapidFRET Integrated Workstation. The assay is used to perform a qualitative screen for amphetamine at 50 ng/mL in neat oral fluid samples collected with the RapidEASE Oral Fluid Collector. This assay provides only a preliminary result. To obtain a confirmed analytical result, a more specific alternate chemical method such as GC/MS or LC/MS/MS is required. Professional judgment should be applied to any drug test result, particularly when using preliminary positive results. For In Vitro Diagnostic Use Only.

The RapidFRET Oral Fluid Calibrator Set and RapidFRET Oral Fluid Control Set are intended for use only with the RapidFRET Oral Fluid Assay for Amphetamine and samples collected with the RapidEASE Oral Fluid Collector. The cutoff calibrator is used to determine the cutoff level and translate the assay measurement into a positive or negative result. The positive and negative controls are used to monitor laboratory systems, operators, precision, accuracy and assay conditions. For In Vitro Diagnostic Use Only.

807.92(a)(6): Technological Similarities and Differences to the Predicate

	Candidate Device (RapidFRET AMP)	**Predicate Device (Roche AMP, K110446)**
Indications for Use	Qualitative determination of amphetamine in human oral fluid in clinical setting.	Qualitative and semi-quantitative determination of amphetamine in human oral fluid in clinical setting.
Methodology	Competitive homogeneous immunoassay.	Competitive homogeneous immunoassay.
Kit Components	1 Drug specific antibody reagent in liquid, ready to use format. 1 Drug conjugate reagent in liquid, ready to use format.	1 Drug specific antibody reagent in liquid, ready to use format. 1 Drug conjugate reagent in liquid, ready to use format.
Performance Characteristics	Precision, accuracy, cross reacting/interfering studies demonstrate equivalence to the predicate device.	Precision, accuracy, cross reacting/interfering studies are similar to the RapidFRET Oral Fluid Assay for Amphetamine.
Safety and	Demonstrated in bench testing and	Demonstrated in bench testing and

	Candidate Device (RapidFRET AMP)	**Predicate Device (Roche AMP, K110446)**
Effectiveness	described in PI, equivalent to predicate.	described in PI.
Neat Oral Fluid Cutoff Level	50 ng/mL neat oral fluid.	120 ng/mL neat oral fluid using a 40 ng/mL cutoff calibrator to account for sample dilution by collection device.
Platform	RapidFRET Integrated Workstation available exclusively from Biophor Diagnostics, Inc.	Roche Modular P Analyzer
Sample Collection	Neat oral fluid is collected with the RapidEASE Oral Fluid Collector via direct expectoration. No diluent is used and sample is stored in glass sample tube with inert screw cap.	Oral fluid is collected with the Intercept Oral Specimen Collection Device. This device uses an absorbent swab and diluent. Sample is stored in plastic tube with snap cap.
Principle and Procedure	Drugs in the oral fluid sample compete with the drug conjugate donor fluorophore for a fixed number of binding sites on the individual drug antibody acceptor reagents. When acceptor and donor fluorophores are brought into close proximity, through the binding event, fluorescent energy transfer is measured. The amount of drug in the specimen sample is inversely proportional to the assay signal as measured by time resolved fluorescence.	The assay is based on the sample analytes competing with analyte conjugates to antibody coated microparticles for antibody binding sites. The amount of drug in the specimen is directly proportional to the assay signal as measured by absorbance.
Controls and Calibrator Levels	Calibrators are available at 0 ng/mL and 50 ng/mL. Controls are available at 25 ng/mL and 75 ng/mL.	Calibrators are available at 0 ng/mL and 40 ng/mL for qualitative mode. Controls are available at 20 ng/mL (0.5X) and 60 ng/mL (1.5X) levels.

807.92(b)(1): Brief Description of Study Data:

A series of studies were performed that evaluated the device performance characteristics including precision and analytical sensitivity, correlation with GC/MS and LC/MS/MS, cross reactivity, and analytical specificity that are summarized below.

Precision and Analytical Sensitivity

Three lots of the RapidFRET Oral Fluid Assay for Amphetamine were analyzed, four times daily, for a minimum of 20 days. Negative oral fluid pools were spiked with amphetamine at 0%, 25%, 50%, 75%, 100%, 125%, 150%, 175% and 200% of the cutoff level corresponding to approximately 0, 12.5, 25, 37.5, 50, 62.5, 75, 87.5 and 100 ng/mL. Spiked oral fluid was then processed with a RapidEASE Oral Fluid Collector prior to analysis. The aggregate data is

summarized in the table below:

All Lots Precision Results Summary by Percent Agreement									
	0%	25%	50%	75%	100%	125%	150%	175%	200%
POS	0%	0%	0%	0%	67%	100%	100%	100%	100%
NEG	100%	100%	100%	100%	36%	0%	0%	0%	0%
N	279	279	278	279	279	278	263	294	278

Correlation with MS Quantitation

Neat oral fluid was collected with the RapidEASE Oral Fluid Collection Device from volunteers potentially positive and negative for amphetamine. The samples (n=415) were randomized and blinded to the instrument operator and assayed using RapidFRET AMP reagents. Following screening, positive and negative samples were sent for confirmatory testing. The summarized data are shown below.

Combined Accuracy Data – Detailed Grouping.				
N = 415	Negative by the predicate device or less than half the cutoff concentration by MS analysis	Near Cutoff Negative (Between 50% below the cutoff and the cutoff concentration)	Near Cutoff Positive (Between the cutoff and 50% above the cutoff concentration)	High Positive (greater than 50% above the cutoff concentration)
Positive	14*	0	6	35
Negative	321	37	2**	0

*Of the fourteen samples, twelve samples contained MDA above the cutoff equivalent cross reactivity level (in ng/mL: 151, 113, 109, 93, 90, 82, 73, 70, 56, 51, 51, and 51). The remaining two samples contained high levels of Dimethylcathinone (DMC), a metabolite of the designer drug dimethylmethcathinone and member of the cathinone class of drugs that share significant structural similarities to amphetamine.[1] **Samples contained 71.6 ng/mL and 70.3 ng/mL amphetamine.

The data indicate that the RapidFRET Oral Fluid Assay for Amphetamine was accurate 99% of the time in neat oral fluid samples collected with the RapidEASE Oral Fluid Collector.

Cross Reactivity and Analytical Specificity

A compound library of approximately 167 different structurally related and unrelated compounds including metabolites, over-the-counter and prescription medications and other drugs of abuse was used to evaluate cross reactivity and interference. Structurally related compounds were spiked at 30,000 ng/mL into neat oral fluid pool aliquots with 0 ng/mL amphetamine for cross-reactivity determinations, and structurally unrelated compounds were spiked at 30,000 ng/mL into neat oral fluid pool aliquots with 25 ng/mL and 75 ng/mL of amphetamine for interference determinations. All samples were processed with the RapidEASE Collector and tested with the RapidFRET AMP assay.

No interference was seen with the tested structurally unrelated compounds. The list of compounds that do not interfere with the assay are listed in the product insert.

For cross-reactivity, the compounds that gave an unexpected result were further titrated to

[1] Usui, K., Aramamaki, T., et. Al., *Legal Medicine*, 16, (2014), 222 -226.

determine the concentration at which the cross-reacting compound yielded a result approximately equivalent to the cutoff. The cross-reactivity of structurally related compounds are summarized below.

Cross-Reactivity Data			
Compound	**Level (ng/mL)**	**Cutoff Equivalent Concentration**	**Percent Cross-Reactivity**
Benzodioxolylbutanamine	30,000	388 ng/mL	13%
Phenethylamine	30,000	5,500 ng/mL	0.9%
Methylenedioxyamphetamine (MDA)	30,000	95 ng/mL	53%
Methylenedioxyethylamphetamine (MDEA)	30,000	24,167 ng/mL	0.2%
Methylenedioxymethamphetamine (MDMA)	30,000	NEG	0.0%
Phentermine	30,000	1,789 ng/mL	2.8%
para-Methoxyamphetamine (PMA)	30,000	533 ng/mL	9.4%
l-Amphetamine	30,000	4,987 ng/mL	1.0%
d-Amphetamine	3,750	50 ng/mL	100%
d/l-Amphetamine	60,000	118 ng/mL	42.4%
d-Methamphetamine	30,000	NEG	0.0%
l-Methamphetamine	30,000	NEG	0.0%
Ephedrine	30,000	NEG	0.0%

A second study evaluated common substances such as foods and dental products as well as pH variations. HSA, ethanol, baking soda, whole blood, hemoglobin, hydrogen peroxide, sodium chloride, cholesterol, denture adhesive, ascorbic acid, bilirubin, IgA, IgG, IgM and salivary α-amylase were spiked into neat oral fluid pool aliquots that contained either 25 ng/mL or 75 ng/mL of *d*-amphetamine. Neat oral fluid pool was titrated to pH values of 5, 6, 7, 8 and 9, spiked with *d*-amphetamine to 25 ng/mL or 75 ng/mL and assayed with the RapidFRET AMP Assay. The effects of antiseptic mouthwash, cough syrup, cranberry juice, orange juice, tooth paste, chewing tobacco, cigarettes, chewing gum, hard candy, teeth whitening strips, cola, water, antacid, coffee and tea were evaluated by asking volunteers to use a specific item and provide an oral fluid sample. These samples were then spiked with *d*-amphetamine to 25 ng/mL or 75 ng/mL, processed with a RapidEASE Collector and assayed with the RapidFRET AMP device. All compounds at the listed concentrations gave a NEG result when spiked with 25 ng/mL *d*-amphetamine and a POS result when spike with 75 ng/mL *d*-amphetamine.

807.92(b)(3): Conclusions

The RapidFRET Oral Fluid Assay for Amphetamine including the RapidFRET Oral Fluid Negative and Cutoff Calibrators, the RapidFRET Oral Fluid Negative and Positive Controls and the RapidEASE Oral Fluid Collector were determined to be safe and effective for their intended use.